Pre-clinical modeling of CCR5 knockout in human hematopoietic stem cells by zinc finger nucleases using humanized mice.

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Public Summary:
Genetic strategies to block expression of CCR5, the major co-receptor of HIV-1, are being developed as anti-HIV therapies. For example, human hematopoietic stem/precursor cells (HSPC) can be modified by the transient expression of CCR5-targeted zinc finger nucleases (ZFNs) to generate CCR5-negative cells, which could then give rise to HIV-resistant mature CD4+ T cells following transplantation into patients. The safety and anti-HIV effects of such treatments can be evaluated by transplanting ZFN-treated HSPC into immunodeficient mice, where the extent of human cell engraftment, lineage differentiation and anti-HIV activity arising from the engineered HSPC can be examined. In this way, humanized mice are providing a powerful small animal model for pre-clinical studies of novel anti-HIV therapies.

Scientific Abstract:
Genetic strategies to block expression of CCR5, the major co-receptor of human immunodeficiency virus type 1 (HIV-1), are being developed as anti-HIV therapies. For example, human hematopoietic stem/precursor cells (HSPC) can be modified by the transient expression of CCR5-targeted zinc finger nucleases (ZFNs) to generate CCR5-negative cells, which could then give rise to HIV-resistant mature CD4(+) T cells following transplantation into patients. The safety and anti-HIV effects of such treatments can be evaluated by transplanting ZFN-treated HSPC into immunodeficient mice, where the extent of human cell engraftment, lineage differentiation and anti-HIV activity arising from the engineered HSPC can be examined. In this way, humanized mice are providing a powerful small animal model for pre-clinical studies of novel anti-HIV therapies.